

Autism Linked to Increased Hip Fracture Risk

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HOUSTON — Children and adults with autism spectrum disorder (ASD) show a significantly higher risk for hip fracture than do those without autism, confirming suspicions raised by previous research showing a link between ASD and lower bone mineral density (BMD).

"In patients with ASD who have low bone density, every effort should be made to identify and treat contributing factors," coauthor Madhusmita Misra, MD, MPH, an associate professor of pediatrics at Harvard Medical School and the Pediatric Endocrine and Neuroendocrine Units at Massachusetts General Hospital in Boston, told *Medscape Medical News*.

"In addition, it may be important to monitor bone density at regular intervals, particularly in older women with ASD, who appear to be at the highest risk for fracture, and those on specialized diets, such as the gluten-free and casein-free diet."

The findings were presented here at American Society for Bone and Mineral Research (ASBMR) 2014.

Growing Evidence Base

Dr Misra's team has previously shown that peripubertal boys with ASD have markedly lower BMD at the spine and hip than typically developing boys of the same age, and important differences were also observed in factors known to affect bone accrual, including calcium and vitamin D intake, physical activity, and cortisol levels.

The new study is the first to take the research a step further and assess fracture risk in autism. For the study, Dr Misra and her colleagues evaluated data from the National Emergency Department Sample 2010 on 18,152 children aged 3 to 22 years with ASD and 4215 adults aged 23 to 50 years with ASD.

The data were evaluated during the course of a year and were compared with data on 6,311,505 children and 11,438,194 adults without ASD in the sample.

The findings showed that the risk for hip fracture in the 3- to 22-year-old population was more than 3 times higher among those with ASD than among individuals without ASD (odds ratio [OR], 3.33; $P < .0001$).

Among girls with ASD, the risk was notably higher than for girls without ASD (OR, 8.1; $P = .0005$) and somewhat higher than for boys with ASD (OR, 2.0; $P = .06$).

A reverse association was seen, however, in terms of upper extremity fractures in boys — boys with ASD had a significantly lower risk for upper extremity fractures than boys without ASD ($P < .0001$).

Adults with ASD similarly showed an increased OR of hip fracture compared with those without the disorder (OR, 11.7; $P < .0001$); likewise, the risk among women was higher (OR, 24.8; $P < .0001$) than for men (OR, 6.8; $P < .0001$).

Adult women with ASD also had a higher risk for upper extremity fractures than did those without ASD (OR, 2.27; $P = .0038$), as well as for spine fractures (OR, 10.61; $P = .0034$). However, adult men with ASD, as seen in boys with ASD, had a lower risk for upper extremity fractures and no increase in the risk for spine fractures.

"It was a surprise to find the higher odds ratio for hip fracture in girls, and for hip, forearm, and spine fracture in women with ASD," Dr Misra said.

"It is difficult to speculate on the reason for this higher odds ratio in girls and women without a systematic evaluation of bone density and its determinants in females with ASD," she added. "We hope to conduct these studies going forward."

The authors did not control for medications that could affect bone, owing to limitations in the data that were available. However, the findings were significant after adjusting for age groups.

Patients receiving antiseizure medications and other medications known to affect bone were excluded in the previous study.

The findings are important in shedding light on a lesser-known health risk associated with autism, which can have significant potential implications.

"A higher risk for fracture, particularly for fractures associated with significant morbidity, such as hip and spine fracture, is concerning in this population, given difficulties expressing pain, sitting still, and cooperating with the intense rehabilitative therapies after surgery," Dr Misra said.

"And because ASD is increasing in prevalence — 1 in 68, based on the CDC 2014 data — a higher risk of fracture could lead to significant healthcare costs and thus further burden our healthcare system."

Brain, Bone Link

Although the BMD deficits seen with ASD have been attributed to various factors, including adverse effects of medications, dietary restrictions, and decreased exercise, recent research has focused more on changes in the nervous system, according to Ronald Y. Kwon, PhD, an assistant professor of orthopedics and sports medicine at the University of Washington in Seattle.

"Over the last decade, a large body of studies has accumulated demonstrating the potential for nerves to directly regulate bone cell activity," he told *Medscape Medical News*.

"We now know that certain regions of the central nervous system, such as the hypothalamus and brain stem, are important for regulating bone metabolism, bringing forth the question of whether other regions of the brain, such as the cerebral cortex, may also be involved."

Dr Kwon and colleagues at the University of Washington and Baylor University have delved into that association in research involving animal models of epilepsy, autism, and other neurologic disorders.

A study involving mice with epilepsy, presented by Dr Kwon and his colleagues at the ASBMR meeting, in fact showed skeletal deficits even when the gene knocked out is targeted primarily to the brain instead of the bone.

"Thus, we believe that the use of genetic models of epilepsy may be a powerful approach for identifying links between the cerebral cortex and bone, and we are now using this and other strategies to determine how this crosstalk occurs," Dr Kwon said.

Dr Misra and Dr Kwon report no relevant financial relationships.

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